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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,333	11/14/2003	Anastasia Khvorova	DHARMA 0100-US2	6379
23719 7590 06/22/2007 KALOW & SPRINGUT LLP 488 MADISON AVENUE 19TH FLOOR NEW YORK, NY 10022			EXAMINER EPFS FORD, JANET L	
			ART UNIT 1633	PAPER NUMBER
			MAIL DATE 06/22/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/714,333

Applicant(s)

KHVOROVA ET AL.

Examiner

Janet L. Epps-Ford

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 07 May 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1 and 38-85 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1, 38-42, 61-78, and 80-83 is/are allowed.
- 6) ☒ Claim(s) 43-60, 79, 84 and 85 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## DETAILED ACTION

### *Response to Amendment*

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 43-60, 79, and 84-85 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's arguments filed 5-07-07 have been fully considered but they are not persuasive.

4. Claim 43 (and those claims dependent therefrom) recites: "a method for *selecting* a siRNA *molecule* for a target gene..." in the preamble. However, in step (d) the claimed method comprises wherein a *candidate siRNA sequence is selected*, and in step (e) *said siRNA molecule is synthesized*. It appears that the preamble of the claimed method is inconsistent with the final outcome of the claimed method, since the final step of the method recites synthesizing an siRNA molecule for a target gene, and not selecting an siRNA molecule for a target gene. Additionally, it is noted that step (b) of the claimed method recites applying to each of said candidate siRNA sequences a *set* of one or more criteria, however in step (d) of the method the claim recites that a siRNA sequence is selected if a candidate siRNA sequence satisfies one or more

criteria. The use of the term "set of one or more criteria.." is not repeated in step (d), moreover it is unclear if the term "set" is intended to encompass more than one criteria, or if it is intended to include wherein only one criteria is applied.

5. Applicant's arguments filed 5-07-07 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the following grounds (see page 17, 1<sup>st</sup> paragraph of the response filed 5-07-07):

First, the Examiner rejects claims 55 – 57 and asserts that there is insufficient antecedent basis for the criteria of GC content, the presence of at least 2A or U bases at position 15 –19 and an internal repeat that is not stable at greater than 50 °C. Applicants have amended each of these claims to clarify that these three criteria are part of group of criteria within a set of criteria that are to be applied to the candidate siRNA sequence is selected. (Applicants have also changed the reference for the 2A or U bases to positions 1 – 5 of the antisense sequence.) Applicants note that although the set of criteria has been increased from that recited in claim 43, so too has then number of criteria that must be applied.

First, contrary to Applicant's assertions, it is noted that the number of criteria that must be applied has increased, however there is support for this limitation in claim 43, wherein it recites "a set of one or more criteria." However, the additional criteria mentioned in claims 55-56 are not supported in independent claim 43. Therefore, the additional criteria lack sufficient antecedent basis.

6. Moreover, in regards to the rejection of claims 55-56, Applicants amended the claims to address the rejection set forth in the prior Office Action. However, contrary to Applicant's assertions, it remains that claims 55-56 recite the criteria selected from the: the presence of...a GC content of between about 30% and 52%, at least 2A or U bases at positions 1-5 of the antisense sequence, and a internal repeat that is not stable at

greater than 50°C. However, as stated in the prior Office Action, instant claim 43 does not provide sufficient antecedent basis for these limitations in the claims.

7. Claims 55-57, and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 55-57, and 60, recite the phrase "an internal repeat that is not stable at a temperature of greater than 50°C." The metes bounds of this phrase are vague and indefinite since it is unclear what it means for an internal repeat to be stable. It is unclear if the phrase is intended to encompass wherein the internal repeat forms a duplex with the target that is not stable at greater than 50°C.

8. Claims 55-57 and 60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (written description).

Claims 55-57, and 60, recite the phrase "an internal repeat that is not stable at a temperature of greater than 50°C." The nucleotide sequence structure of this internal repeat is not properly described in the specification as filed, or in the instant claims. Moreover, it is noted that the nucleotide sequence structure of siRNA molecules comprising internal repeats that are not stable at a temperature greater than 50°C must be empirically identified. Furthermore, if the term "stable" as used in these claims is in reference to the stability of a duplex formed with the internal repeat, the identity of the

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target sequence is not identified, therefore the stability is not defined relative to a single SEQ ID NO which is being varied within limits of similarity or hybridization, it is based on apparently any sequence with an internal repeat that is not stable at a temperature of greater than 50oC.

See MPEP § 2163, which states "[A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence."

See also the January 5, 2001 (Vol. 66, No. 4, pages 1099-1111) Federal Register for the Guidelines for Examination of Patent Applications Under the 35 USC 112 ¶ 1, "Written Description" Requirement. These guidelines state: "[T]o satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing

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identifying characteristics sufficient to show that applicant was in possession of the claimed invention."

Since it appears that the nucleotide sequence structure of the claimed sequences having "an internal repeat that is not stable at a temperature of greater than 50°C," must be identified by further experimentation, it is concluded that applicants were not in possession of the full scope of the claimed invention as of the filing date of the instant invention.

***Conclusion***

9. Claims 1, 38-42, 61-78, and 80-83 are allowable over the prior art searched.
10. Claims 43-60, 79, and 84-85 are rejected for the reasons set forth above.

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11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Ford/  
Primary Examiner  
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JLE